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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Charles V. Lowry	Attorney Docket No.:	0410.008
Serial No.:	09/989,534	Group Art Unit:	~~1645~~ 1636
Filed:	November 20, 2001	Examiner:	Lambertson, D.A.

Title: PLASMIDS AND METHODS FOR MONITORING ENDONUCLEASE DIGESTION EFFICIENCY

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Non-Fee Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on May 15, 2003.

Kathy Smith Dias

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Date of Signature: May 15, 2003

To: Mail Stop Non-Fee Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Response to Restriction Requirement Under 37 C.F.R. § 1.142

Dear Sir:

This is in response to the Office Action mailed on April 17, 2003, in connection with the above-identified U.S. patent application. The thirty-day period for response expires on May 17, 2003. Accordingly, this response is timely filed.

Claims 1-41 were presented at the time of filing and are currently pending in the application. The Action of April 17, 2003 requires election under 35 U.S.C. §121 among six groups of claims:

Group I (claims 1-11, 17-18, 29, 33, 34, 38 and 39), drawn to a plasmid for use in monitoring the efficiency of a restriction digest, a method of designing the plasmid and kits containing the single plasmid, classified in class 435, subclass 320.1;

Group II (claims 12-16, 19-21, 22, 33, 35, 38 and 39), drawn to a set of two plasmids for use in monitoring the efficiency of a restriction digest, a method of designing the plasmids and kits containing the set of two plasmids, classified in class 435, subclass 320.1;

Group III (claims 12-16, 19-25, 33, 36, 38 and 39), drawn to a set of three plasmids for use in monitoring the efficiency of a restriction digest, a method of designing the plasmids and kits containing the set of three plasmids, classified in class 435, subclass 320.1;

Group IV (claims 12-16, 19-22, 26-28, 33, 37-39 and 40, drawn to a set of four plasmids for use in monitoring the efficiency of a restriction digest, in particular the set of plasmids indicated in Figure 1 of the specification of the instant application, and kits containing the set of four plasmids, classified in class 435, subclass 320.1;

Group V (claims 12-16, 19-22, 26-28, 33, 37-39 and 41), drawn to a set of four plasmids for use in monitoring the efficiency of restriction digest, in particular the set of plasmids indicated in Figure 2 of the specification of the instant application, and kits containing the set of four plasmids, classified in class 435, subclass 320.1; and

Group VI (claims 3-32), drawn to a method for monitoring the efficiency of a restriction digest, classified in class 435, subclass 6.

Applicants hereby provisionally elect the claims of Group I (claims 1-11, 17-18, 29, 33, 34, 38 and 39) with traverse.

The examiner has stated that the inventions of Groups I-VI can be shown to be distinct if "it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions or different effects." Applicants respectfully suggest that this statement is wholly inapposite in the present case.

The Office Action states that "the inventions have different functions because each set of plasmids is designed to produce restriction fragments of different sizes in order to ascertain the efficiency of a restriction enzyme." A brief discussion of the invention and its use ensues.

The invention encompasses the use of specifically designed plasmids (hereinafter referred to as "monitor" plasmids) to monitor the efficiency of a restriction endonuclease digestion reaction in which two restriction endonucleases are used to cut a circular plasmid. The problem with digestion, generally, is that the exogenous DNA insert in the plasmid (the DNA between the two restriction sites) usually is so small that it is difficult and in some cases impossible to distinguish, once the plasmids are digested and the digestion products electrophoresed on an agarose gel, between a plasmid which has been cut at only one restriction site (linearized but intact) from one that has been cut at both sites, the difference in size between the two being the size of the very small DNA insert bounded by the restriction sites.

To address this problem, Applicant has devised a method by which the efficiency of a digestion reaction can be monitored by including "monitor" plasmids in the digestion reaction which are specifically designed so that regardless of the combination of two endonucleases used, successful digestion of the "monitor" plasmid (i.e. with both endonucleases) will generate two fragments sufficiently different in size from the intact plasmid so that their migration pattern on an agarose gel differs significantly from a "monitor" plasmid which has been cut at only one site, rendering them easily distinguishable from each other. This is accomplished by placing the restriction sites on the "monitor" plasmid(s) at a distance from each other adequate to ensure that the fragments resulting from digestion are significantly different in size from the merely linearized but intact plasmid. The fragment size is not intended to give any additional information about the restriction endonucleases used, only whether it has cut or not cut the plasmid at its respective site.

It does not necessarily follow that the plasmids have different functions because the nucleotide sequences of the monitor plasmids vary from plasmid to plasmid or from set to set. The nucleotide sequence of the plasmid is only significant in that it provides the necessary restriction site(s) for the cognate endonucleases to cut the plasmid. Larger plasmid sets provide more options in terms of the number of restriction endonucleases that can be monitored; 33-81 sites for the four-plasmid set vs. 27-64 sites for a three-plasmid set. The plasmid sets depicted in Figures 1and 2 represent examples of a two different arrangements of 33 restriction sites so that

for any pair of restriction enzymes, one plasmid of the set will be informative of digestion efficiency. Only one plasmid of a set is chosen to monitor a reaction. Each plasmid contains the same 33 restriction sites, only in an altered arrangement.

All the plasmids, however, function in the same manner regardless of their sequence or their existence in a set. That function is to indicate whether a particular endonuclease digestion has been completed. For a particular digestion reaction using any two endonucleases represented on the "monitor" plasmid, successful digestion yields digestion products that are significantly different in size, have different electrophoretic mobilities and, therefore, are readily distinguishable from a linearized but intact plasmid (incomplete digestion).

With respect to Groups I-V, the plasmids, their design and their use to monitor digestion are the same, regardless of whether it is a single plasmid, a set of such plasmids, or the number of plasmids contained in a set of plasmids; all the plasmids are designed based on the same premise, are used for the same purpose and function in the same fashion.

With respect to the method claims of Group VI, the method cannot be performed with any plasmids other than those claimed in Groups I-V. Thus, of necessity, Group VI claims require use of the plasmid as recited in the claims of Group I or a set of plasmids as recited in the claims of Groups II-V.

Moreover, applicants respectfully suggest that a proper search of the art for Group I will necessarily include all of the art pertinent to Groups II-VI. As a result, applicants believe that there would not be a serious burden on the examiner if restriction is not required [see MPEP §803(2)].

Withdrawal of the restriction between Group I and Groups II-IV is requested.

The Examiner is invited to contact Applicants' Attorney at the telephone number given below, if any further questions arise in connection with this Application.

Respectfully submitted,

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Dated: May 15, 2003

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